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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/776,768	02/06/2001	Stephen P.A. Fodor	56297-5009	3913

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EXAMINER

SIEW, JEFFREY

ART UNIT	PAPER NUMBER
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1637

DATE MAILED: 04/20/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/776,768

Applicant(s)

FODOR ET AL.

Examiner

Jeffrey Siew

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 29 January 2004.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 25-45 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 25-45 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 29 June 2001 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Claim Rejections - 35 USC § 112

1. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 25-45 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A) The term “comprising a single nucleotide variation” is confusing and renders claims 25-45 indefinite. It is unclear as to whether the probe only contains single nucleotide variation as compared to the known core probe sequence. The term “comprising” is open language and would appear to suggest that the probe may contain multiple mutations which are a plurality of “single nucleotide variations.”

Claim Rejections - 35 USC § 102

2. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless --

(e) the invention was described in-

(1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in

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section 351(a) shall have the effect under this subsection of a national application published under section 122(b) only if the international application designating the United States was published under Article 21(2)(a) of such treaty in the English language; or

(2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that a patent shall not be deemed filed in the United States for the purposes of this subsection based on the filing of an international application filed under the treaty defined in section 351(a).

Claims 25-27,30-37, 39 , 42 & 45 are rejected under 35 U.S.C. 102(e) as being anticipated by Southern et al (6,054,270 April. 25, 2000).

Southern teach a method of detecting a mutation in target nucleic acid versus a known sequence comprising screening target sequence by exposing target sequence to at least one known core sequence probe, determining absolute binding affinity of target sequence to known core sequence probe thereby detecting mutation (see whole doc. esp. abstract & example 3 “array with multiple oligonucleotides including 19mer oligonucleotide compare hybridization affinity against a temperature gradient thereby detecting mismatches”). They detect thru scanning autoradiographic images (see col. 8 line 45-53). They also teach 11, 12 and 13 oligomers (see col.9 line 42). They teach detection of sickle cell anemia mutation (see Example 4 & col.11 lines 6-15 where target β -globin gene is screened), The teach detection of cystic fibrosis (see col.3 line 8).

The terms “core sequence probe” and absolute binding affinity” read broadly on Southern’s array probes and his measurement of resulting hybridization of targets .

The response filed 4/17/04 has been fully considered and upon further review deemed not persuasive. The response states that claims have been amended to recite one probe comprising a single nucleotide variation of at least one know core sequence probe and that Southern et al do not teach any “known” core sequence probes”, “determining binding affinity” or “comparing binding affinity of known core sequence probe to target and a known sequence”. First, the term “probe comprising a single nucleotide variation” has been cited under 112 second paragraph for

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indefiniteness (see *supra*). The term when read broadly and reasonably would still encompass Southern et al's different varied probes. Moreover the terms "known core sequence probes" and "binding affinity" are applicants chosen words. A review of the instant application does not reveal any particular limitation or definition to such terms. As such the terms are interpreted in their logical and commonly known meanings to one skilled in the art. Southern et al oligonucleotide probes particularly the wild type probes would satisfy the limitation of known core sequence as the sequences of the wild type probes were known and constructed to hybridize to the wild type target. Second, Southern's measure of the complementariness of two strands in the process of hybridization during the melting is a measure of binding affinity. The instant specification does not particularly limit the term to a specific type or methodology of measurement. Moreover Southern do teach a comparison of probes with targets over a temperature range (see col. 10 lines 55-65).

The response further argues that Southern do not teach the same determination of binding affinity as required in the instant claims because Southern et al relies on detecting only perfectly matched sequence targets and that there is no comparison of binding affinities. However, Southern does a comparison between the differently matched targets and compares their melting behavior (see col. 11 line 25-30). The claims read broadly and would encompass Southern et al's measure of hybridization using melting temperatures to distinguish mismatches. The melting behavior measures the level of complementariness between the strands which in turn is a measure of their binding affinity. The art rejections over principal Southern rejections are therefore maintained.

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Claim Rejections - 35 USC § 103

3. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claim 38 are rejected under 35 U.S.C. 103(a) as being unpatentable over Southern (6,054,270 April. 25, 2000) in view of Shuber (US5,633,137 May 27 1997).

The teachings of Southern are described previously.

Southern do not teach P-53.

Shuber teach ASO probes for detection of mutations in P-53 (see whole doc. esp. col.1 line37 & col.4 line 19).

One of ordinary skill in the art would have been motivated to apply Shuber's probes to Southern et al's array in order to detect mutations in P-53 genes. As Shuber explicitly teach the different sequences of probes to detect disease mutations in P-53, a reasonable expectation of

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success would exist in applying these probes to Southern's oligonucleotide array. It would have been prima facie obvious to combine Southern's array and Shuber et al's probe in order to screen and detect the mutations in disease gene sequence in target samples.

4. Claims 40 & 41 are rejected under 35 U.S.C. 103(a) as being unpatentable over Southern et al (6,054,270 April. 25, 2000) in view of Owerbach (US4,965,189 Oct 23, 1990).

The teachings of Southern are described previously.

Southern do not teach DQ-beta gene.

Shuber teach probes for detection of mutations in DQ beta gene (see whole doc. esp. abstract).

One of ordinary skill in the art would have been motivated to apply Owerbach probes to Southern et al's array in order to detect mutations in DQ-Beta genes. As Owerbach explicitly teach the different sequences of probes to detect disease mutations in DQ-beta gene, a reasonable expectation of success would exist in applying these probes to Southern's oligonucleotide array. It would have been prima facie obvious to combine Southern's array and Owerbach's probe in order to screen and detect the mutations in DQ-beta gene sequence that show a predisposition to diabetes mellitus in individuals.

5. Claims 43 is rejected under 35 U.S.C. 103(a) as being unpatentable over Southern et al (6,054,270 April. 25, 2000) in view of Erlich et al (US5,468,613 Nov. 21, 1995).

The teachings of Southern are described previously.

Southern do not teach DQ-beta gene.

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Southern do not teach forensics.

Erlich et al teach probe hybridization in forensic analysis.(see whole doc. esp. col4 line 53).

One of ordinary skill in the art would have been motivated to apply Erlich et al' teaching of forensic applications to Southern's hybridization assay in order to perform forensic analysis on individuals. As Erlich teach that polymorphic determinations are useful for forensic analysis, it would have been prima facie obvious to combine Erlich et al's motivation to determine sequences in forensic analysis to Southern's array which identify individuals.

6. Claims 28 & 29 are rejected under 35 U.S.C. 103(a) as being unpatentable over Southern et al (6,054,270 April. 25, 2000) in view of Fodor et al (US5,324,633 June 28, 1994).

The teachings of Southern are described previously.

Southern do not teach plotting and normalization.

Fodor et al teach plotting the binding affinity results of fluorescence assays on graph and normalized. (see col.7 line 9-26 & Figure 6).

One of ordinary skill in the art would have been motivated to apply Fodor et al's teachings of fluorescence plots to Southern's array results in order to plot the binding affinity of the probes with targets. As it was well known and commonly practiced in the art to plot the data results, it would have been prima facie obvious to apply Fodor et al's teaching of normalized plots to Southern probe arrays in order to examine the binding results of the different probes and correlate with the target sequence.

SUMMARY

7. No claims allowed.

CONCLUSION


8. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jeffrey Siew who can be reached at 571-272-0787. The e-mail address is Jeffrey.Siew@uspto.gov. However, the office cannot guarantee security through the e-mail system nor should official papers be transmitted through this route. The examiner is on flex-time schedule and can best be reached on weekdays from 6:30 a.m. to 3 p.m. If attempts to reach the examiner are unsuccessful, the examiner's supervisor, Gary Benzion, can be reached on (571)272-0782.

Any inquiry of a general nature, matching or filed papers or relating to the status of this application or proceeding should be directed to the Tracey Johnson for Art Unit 1637 whose telephone number is (571)272-0534.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The 1600 Tech Center FAX is (703)-872-9306.


JEFFREY SIEW
PRIMARY EXAMINER

April 17, 2004